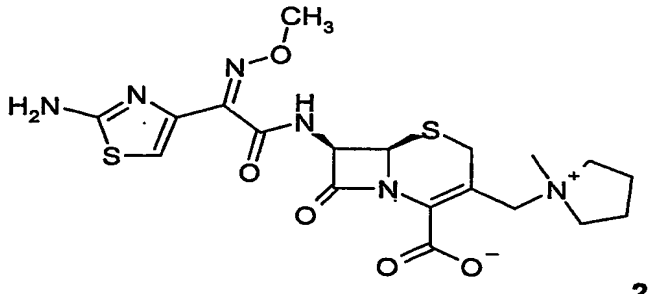
Claims

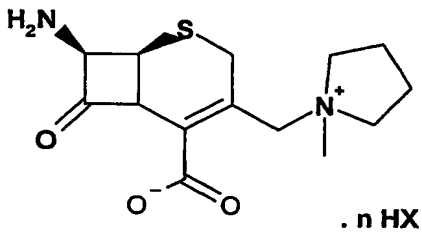
1. A process for producing a compound of formula I

I



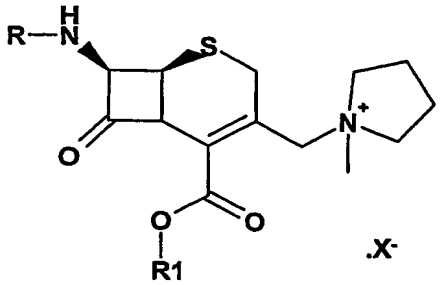
. 2 HCl . H_2O

wherein a compound of formula IIA or IIB



II A

. n HX



II B

.X-

wherein

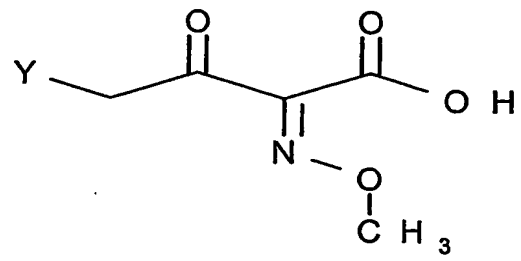
R_1 is a trialkylsilyl group,

R is hydrogen or a trialkylsilyl group,

n is 0 - 2 and

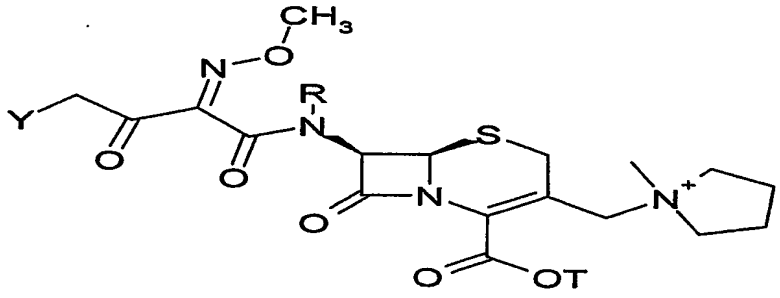
X signifies chloride, bromide or iodide

is reacted with a reactive derivative of formula III



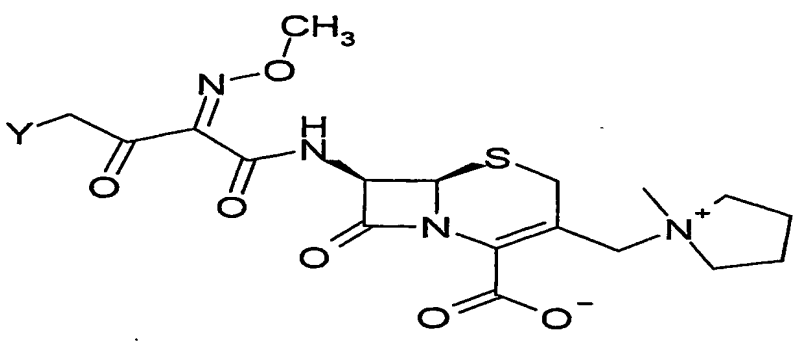
III

wherein Y signifies halogen or a leaving group, to form a compound of formula IV or V



IV

wherein T is trialkylsilyl, the silyl protecting groups, if present, are removed , or the compound of formula IV as the acid addition salt of formula V is isolated wherein m is 0 or 1 and the compound of formula IV



V

or the compound of formula V is cyclised with thiourea, and subsequently the compound of formula I is isolated.

2. A process as claimed in claim 1, wherein the compounds of formula II are produced from their respective mono- or di- hydrogen halide adducts.

3. A process as claimed in claim 1 or 2, wherein pyrrolidinium-1-[(7-amino-2-carboxy-8-oxo-5-thia-1-azabicyclo[4.2.0]oct-2-en-yl)methyl]-iodide monohydrate is used.

4. A process as claimed in claim 1 or 2, wherein pyrrolidinium-1-[(7-amino-2-carboxy-8-oxo-5-thia-1-azabicyclo[4.2.0]oct-2-en-yl)methyl]-chloride or pyrrolidinium-1-[(7-amino-2-carboxy-8-oxo-5-thia-1-azabicyclo[4.2.0]oct-2-en-yl)methyl]-dihydrochloride is used, optionally in solvated form.

5. A compound of formula V, wherein Y and X are Cl.

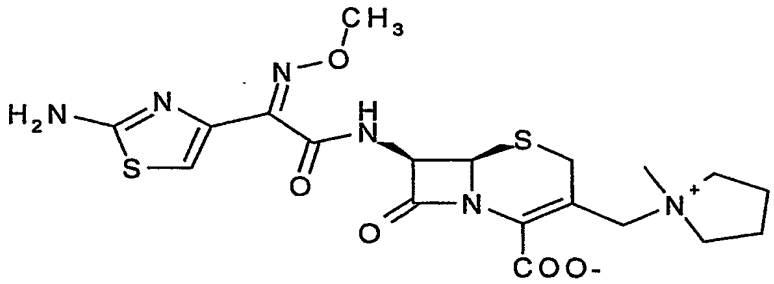
6. A compound as claimed in claim 5 in crystalline form wherein the compound of formula V is in free base or acid addition salt form.

7. A compound as claimed in claim 6 having an X-ray powder diffraction pattern substantially as that shown in Figure 1 or Figure 2.

8. A process according to claim 1, characterised in that 4-chloro-2-methoxyimino-3-oxo-butyryl chloride is used as the reactive derivative of formula III.

9. A process as claimed in any of claims 1 to 5 or 8, wherein prior to precipitation or crystallisation of the compound of formula I, any bromide or iodide ions that may be present are removed by ion exchange.

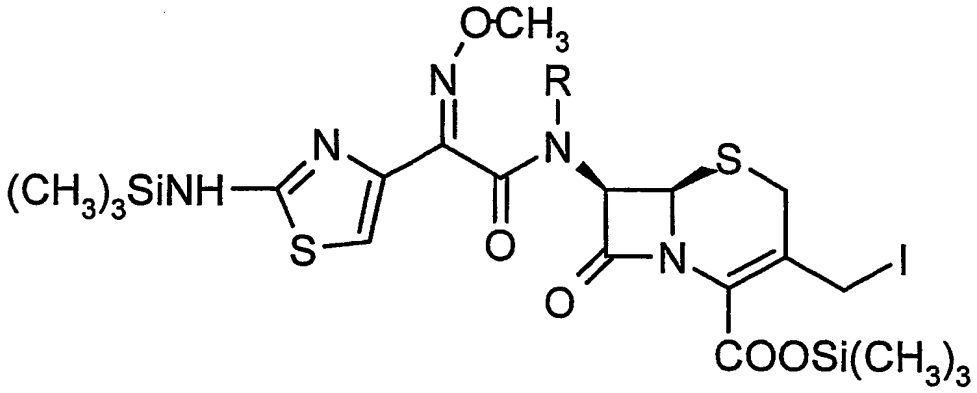
10. A process for producing the compound of formula I



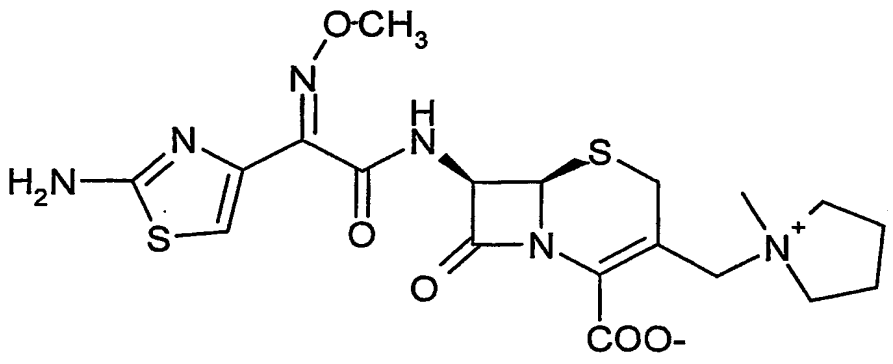
I

. 2 HCl . H_2O

characterised in that a compound of formula VIII



is desilylated in a protic solvent, and subsequently reacted with N-methylpyrrolidine to form a compound of formula X, and this is then converted into the compound of formula I

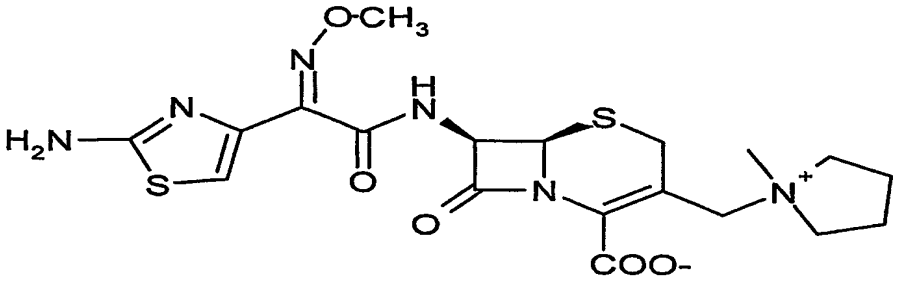


X . HI

11. A process as claimed in claim 10, wherein the protic solvent is a C_1-C_4-alcohol.

12. A process according to claim 10 or 11, wherein conversion of the compound of formula VIII is effected using a basic ion exchanger.

13. A process as claimed in claim 10, 11 or 12, wherein conversion of the compound of formula X into the compound of formula I is effected through the free betaine of formula XI in isolated form

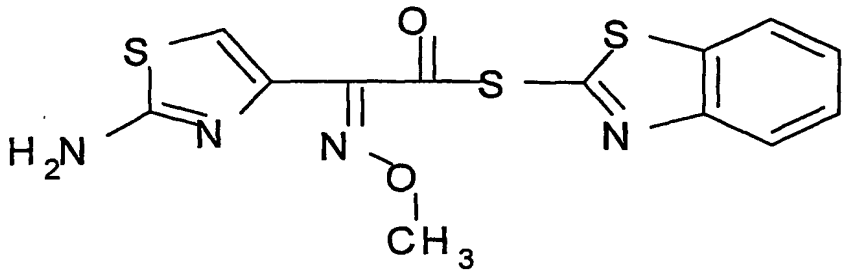


XI .

14. A process for producing the compound of formula I

characterised in that a compound of formula IIA, in unsolvated or solvated form, is reacted optionally after addition of a base, with a compound of formula XII

XII



in acetone or aqueous acetone, and the compound of formula I precipitated in crystalline form from the reaction mixture by adding HCl.

15. A process as claimed in claim 14, wherein pyrrolidinium-1-[(7-amino-2-carboxy-8-oxo-5-thia-1-azabicyclo[4.2.0]oct-2-en-yl)methyl]-iodide monohydrate is used.

16. A process as claimed in claim 14, wherein pyrrolidinium-1-[(7-amino-2-carboxy-8-oxo-5-thia-1-azabicyclo[4.2.0]oct-2-en-yl)methyl]-chloride is used, optionally in solvated form.

17. A process as claimed in claim 14, wherein pyrrolidinium-1-[(7-amino-2-carboxy-8-oxo-5-thia-1-azabicyclo[4.2.0]oct-2-en-yl)methyl]-dihydrochloride is used, optionally in solvated form.

18. A process as claimed in any one of claims 14 to 17, wherein a C_1-C_8-trialkylamine, KOH or NaOH, or an alkali hydrogen carbonate or potassium carbonate, is used as the base.